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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/562,627 | 12/22/2005 | Mu-Hyeon Choe | 428.1060 | 6450 |

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| EXAMINER | |
|---|---|
| KOSSON, ROSANNE | |
| **ART UNIT** | **PAPER NUMBER** |
| 1652 | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/562,627 | CHOE ET AL. | |
| | Examiner | Art Unit | |
| | Rosanne Kosson | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 October 2006*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *21-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *21-47* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1, claim(s) 21, 27, 30 and 39, drawn to a fusion protein monomer comprising a functional domain that is an enzyme, an extension peptide containing a C residue and a binding domain.

Group 2, claim(s) 21 and 27-30, drawn to a fusion protein monomer comprising a functional domain that is a toxin, an extension peptide containing a C residue and a binding domain.

Group 3, claim(s) 21, 27 and 30, drawn to a fusion protein monomer comprising a functional domain that is a virus having a cationic tail for gene therapy, an extension peptide containing a C residue and a binding domain.

Group 4, claim(s) 21, 27 and 30, drawn to a fusion protein monomer comprising a functional domain that is a drug, an extension peptide containing a C residue and a binding domain.

Group 5, claim(s) 21, 27 and 30, drawn to a fusion protein monomer comprising a functional domain that is a drug delivery liposome, an extension peptide containing a C residue and a binding domain.

Group 6, claim(s) 21, 27 and 30, drawn to a fusion protein monomer comprising a functional domain that is a biosensor for real time detection of target molecules, an extension peptide containing a C residue and a binding domain.

Group 7, claim(s) 22-27 and 30, drawn to a monomer fusion protein comprising a first portion comprising one or more first binding domains, one of which is covalently bound to an extension peptide containing a C residue, and a second portion comprising a second binding domain covalently bound to a linker peptide, which is covalently bound to a functional domain that is an enzyme.

Group 8, claim(s) 22-30, drawn to a monomer fusion protein comprising a first portion comprising one or more first binding domains, one of which is covalently bound to an extension peptide containing a C residue, and a second portion comprising a second binding domain covalently bound to a linker peptide, which is covalently bound to a functional domain that is a toxin.

Group 9, claim(s) 22-27 and 30, drawn to a monomer fusion protein comprising a first portion comprising one or more first binding domains, one of which is covalently bound to an extension peptide containing a C residue, and a second portion comprising a second binding domain covalently bound to a linker peptide, which is covalently bound to a functional domain that is a virus having a cationic tail for gene therapy.

Group 10, claim(s) 22-27 and 30, drawn to a monomer fusion protein comprising a first portion comprising one or more first binding domains, one of which is covalently bound to an extension peptide containing a C residue, and a second portion comprising a second binding domain covalently bound to a linker peptide, which is covalently bound to a functional domain that is a drug.

Group 11, claim(s) 22-27 and 30, drawn to a monomer fusion protein comprising a first portion comprising one or more first binding domains, one of which is covalently bound to an extension peptide containing a C residue, and a second portion comprising a second binding domain covalently bound to a linker peptide, which is covalently bound to a functional domain that is a drug delivery liposome.

Group 12, claim(s) 22-27 and 30, drawn to a monomer fusion protein comprising a first portion comprising one or more first binding domains, one of which is covalently bound to an extension peptide containing a C residue, and a second portion comprising a second binding domain covalently bound to a linker peptide, which is covalently bound to a functional domain that is a biosensor for real time detection of target molecules.

Groups 13-24, claim(s) 37, 38, 41 and 42, drawn to a polynucleotide encoding one of the fusion protein monomers of claims 1-12, a host cell comprising the polynucleotide, and method of producing the polypeptide encoded by the polynucleotide, comprising culturing the host cell. Group 13 corresponds to a polynucleotide encoding the polypeptide of Group 1; Group 14 corresponds to a polynucleotide encoding the polypeptide of Group 2, etc.

Groups 25-48, claim(s) 43-47, drawn to a method of making a homodimer or a method of making a heterodimer, comprising transforming a host cell with a polynucleotide encoding one of the polypeptide monomers of Groups 1-12 or comprising transforming a host cell with a polynucleotide encoding one of the polypeptide monomers of Groups 1-12 and a polynucleotide encoding a second polypeptide, the second polypeptide comprising a binding domain and an extension polypeptide containing a C residue. Group 25 corresponds to making a homodimer of the polypeptide of Group 1; Group 26 corresponds to making the heterodimer of the polypeptide of Group 1; Group 27 corresponds to making a homodimer of the polypeptide of Group 2; Group 28 corresponds to making the heterodimer of the polypeptide of Group 2; etc.

Note:
If one of Groups 1-12 is elected, one of the dimers, either one homodimer or one heterodimer recited in the set of claims 31-36 and 40 will be examined. Regarding claims 31-36 and 40, further restriction is required, as claim 31 is drawn to 144 different dimeric structures, and claim 32 is drawn to an infinite number of heterodimeric structures. Only one dimer from among those recited in claims 31 and 32 combined will be searched and examined. If Applicants elect one of Groups 1-12, the monomer of the elected group will be the first half of the dimer that is

examined. For the second half of the dimer, Applicants must elect either one monomer from Groups 1-12 or the additional fusion protein monomer recited in claim 32.

The inventions listed as Groups 1-48 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons.

The requirement of unity of invention is not fulfilled because there is no technical relationship among these inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" means those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. Therefore, a technical relationship is lacking among the claimed inventions involving one or more special technical features. The technical feature that links all 48 groups of inventions is a fusion protein comprising a first protein domain that is a binding domain, linked to an extension peptide containing a C residue, in which the C residue is 1-45 residues away from the binding domain, linked to a second domain that can be anything. The second domains recited in the claims have no common structures or functions and can be a protein, a virus, a drug, a liposome or a biosensor. The monomers of Groups 1-6 have an extension peptide located between a binding domain and a functional domain, while the monomers of Groups 7-12 have an extension peptide located between two binding domains. Thus, the monomers of Groups 1-6 have different structures and orders of domains than the monomers of Groups 7-12.

The inventions of Groups 1-48 do not share the common special technical feature of a protein that is a binding domain, linked to a C-containing extension peptide, linked to something else, bcause Choe et al. ("B3(Fab)-PE38M: a recombinant immunotoxin in which a mutant form of Pseudomonas exotoxin is fused to the Fab fragment of monoclonal antibody B3," Cancer Res 54:3460-3467, 1994), cited in Applicants' IDS of December 22, 2005, discloses a fusion protein containing a first domain that is a protein and a binding domain (PE38) covalently linked to an extension peptide, either the light chain or the Fd fragment of monoclonal antibody B3. A cysteine residue is 1-45 amino acids away from the first domain. The extension peptide is covalently linked to either the Fd fragment or the light chain of monoclonal antibody B3. That is, the extension peptide and the second domain are reversible domains (see p. 3462, right col.).

Thus, the technical feature of a fusion protein that is a binding domain, linked to a C-containing extension peptide, linked to something else, does not define the invention over the prior art. Because the common technical feature is not novel (special) with respect to the cited reference, it is clear that the claims of Groups 1-48 lack a single common technical feature that defines them over the prior art.

Further, an international application containing claims to different categories of inventions will be considered to have unity of invention if the claims are drawn only to one of certain combinations of categories:
(1) A product and a process specially adapted for the manufacture of said product; or
(2) A product and process of use of said product; or
(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process (see 37 CFR 1.475(b)-(d)). In the instant case, the claims are drawn to multiple products and multiple processes, only a particular combination of which including Group 1 may be considered for unity of invention, i.e., Group 1 and Group 25, (the first named product and the first named process of using the product). Other groups are drawn to additional products and processes, and other combinations do not comply with the aforementioned Rules. But, because a corresponding special technical feature is not present, Groups 1 and 25 cannot be considered to have unity of invention.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows.

a) In claim 21, Applicants must elect one extension peptide from the three listed in part (iii).

b) In claim 22, Applicants must elect one of the extension peptides from the two listed in part (i) and one second protein chain from the two listed in part (ii) .

c) In claim 23, Applicants must elect one definite integer for "n," which will determine the number of additional protein moieties in the elected monomer.

d) In claim 26, Applicants must elect one definite amino acid sequence and one definite integer for "n," so that this sequence that can be searched. Applicants must elect S or A at position 2 and K or Q at position 4.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of

claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The following claim(s) are generic: 21, 22, 23 and 26.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons. Each species has a different structure and different chemical and biological properties, requiring a separate search for each. In claim 23, the number of different protein subdomains in unlimited, resulting in vastly different structures with vastly different functions.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

**Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).**

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rosanne Kosson
Examiner, Art Unit 1652

rk/2007-05-18